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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/025,274	12/19/2001	David N. Herndon	D6197D	5877

52034 7590 05/22/2006

FULBRIGHT & JAWORSKI, L.L.P.
600 CONGRESS AVENUE
SUITE 2400
AUSTIN, TX 78701

EXAMINER	
MARVICH, MARIA	

ART UNIT	PAPER NUMBER
1633	

DATE MAILED: 05/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/025,274	HERNDON ET AL.	
	Examiner	Art Unit	
	Maria B. Marvich, PhD	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 September 2005 and 06 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5-10 and 25-42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *10* is/are allowed.

6)☒ Claim(s) *5-9 and 25-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This office action is in response to an amendment filed 9/16/05 and 3/6/06. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/6/06 has been entered.

Claims 5-10 and 25-42 are pending. Claims 25-42 are newly added.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 5-6 and 9 are rejected under 35 U.S.C 103(a) are rejected under 35 U.S.C. 103 as being unpatentable over Goldstein et al (US Pat No. 5,962,427) taken with McDonald et al (US Pat No. 6,120,799) or Yang et al (Neuroreport, Vol 8, pages 2355-2358, 1997; see entire document). **This rejection is maintained for reasons of record in the office action mailed 5/17/05 and restated below.**

Goldstein et al in the '427 patent directed to a DNA gene therapy method for external wound healing by using a gene activated matrix containing DNA encoding a growth factor teaches that gene activated matrix material including implants, sponges, pads, wound dressings, sutures, dermal patches, cadaver skin are effective matrices for enhancing the migration of wound healing and/or repair cells from surrounding tissues into a wound site that is covered by the matrices containing the therapeutic DNA (entire document, especially column 11, third paragraph, column 12, first paragraph, column 13, third paragraph, column17 bridging column 18, and column 24, last paragraph. A List of growth factors is disclosed on column 14, for example. Goldstein *et al.* does not teach the use of a cholesterol containing cationic as a carrier or vector for the growth factor encoded DNA, nor does Goldstein *et al.* teach explicitly the types of wound dressings or closure materials as recited in the Markush group of the claimed invention.

However, at the time the invention was made, McDonald et al. (column 2 bridging column 3, column 3 bridging column 4, columns 11, 16 and 17) and Petrie et al. (columns 7 and 8) are exemplified references that teach that a therapeutically effective amount of a cholesterol containing cationic liposome is routinely employed in the art as carriers of growth factor encoded DNA so as to enhance gene expression of the delivered DNA in target cells of an external

wound, see column 3 bridging column 4, column 12, lines 10-65, column 16 bridging column 17, column 19, last full paragraph, column 20, last paragraph bridging column 21.

As well, at the time the invention was made, Yang et al review the art of use of DC-cholesterol liposomes for use in delivery of growth factors *in vivo*. Yang et al teach that DC-Chol liposomes have no significant toxicity and are based upon effective delivery using liposome-mediated delivery, which are simple and effective procedures (see e.g. page 2358,col 1,paragraphs 1-2). Yang et al demonstrate that direct administration of the DC-Chol liposomes at target sites lead to no tissue damage and localized expression (see e.g. abstract).

It would have been obvious for one of ordinary skill in the art to have employed cholesterol-containing cationic liposomes as carriers or vectors of the DNA of Goldstein et al. so as to enhance the wound healing process of an external wound (bone rupture, ligament wound, thermal wound, or external wounds as a result of any trauma known in the prior art) in an individual. One of ordinary skill in the art would have been motivated to have employed the liposomes employed in the cited references because McDonald et al and Yang et al are two of many prior arts of record, which teaches that cholesterol-containing cationic liposomes are routinely employed in the art as effective carriers of therapeutic materials or wound enhancing growth factor encoding gene construct to enhance an efficacy of gene expression of the gene construct at its target site.

Thus, the claimed invention as a whole was *prima facie* obvious.

Claims 5, 9, 11, and 15 are rejected under 35 U.S.C 103(a) are rejected under 35 U.S.C. 103 as being unpatentable over Goldstein et al. (US Pat No. 5,962,427) taken with McDonald et

al. (US Pat No. 6,120,799) or Yang et al (Neuroreport, Vol 8, pages 2355-2358, 1997; see entire document), and further in view of Coleman (US 2003/0018984). **This rejection is maintained for reasons of record in the office action mailed 5/17/05 and restated below.**

Goldstein et al. taken with McDonald et al. are applied here as indicated above. Goldstein et al. taken with McDonald et al. do not teach explicitly that a growth factor is IGF-I.

However, at the time the invention was made, Coleman teaches that IGF-I encoding expression vector is effective for use to treat an external wound as a result of a nerve crush, see par. 0007, page 1, and par. 0314, page 27. Cationic liposome used as a DNA carrier is also disclosed on par. 0264 of page 23.

It would also have been obvious for one of ordinary skill in the art to employ an IGF-I encoding gene construct in the wound coverage material of Goldstein et al. taken with McDonald et al. One of ordinary skill in the art would have been motivated to employ an IGF-I as a growth factor gene in the wound dressings and/or wound closure materials as wound healing agents because of the advantages as disclosed in Goldstein taken with McDonald, and because Coleman teaches that IGF-I expressing vector can be used to enhance a muscle healing in damage nerve tissues in an external wound such as a nerve crush.

Thus, the claimed invention as a whole was prima facie obvious.

Claims 5-6, 9, 25-30, 35 and 39-42 are rejected under 35 U.S.C 103(a) are rejected under 35 U.S.C. 103 as being unpatentable over Coffee (US Pat No. 6,252,129; see entire document) taken with McDonald et al. (US Pat No. 6,120,799) or Yang et al (Neuroreport, Vol 8, pages 2355-2358, 1997; see entire document). **This is a new rejection.**

Coffee teaches application of a wound covering material to burn or other injuries in which the matrix delivers growth factors such as fibroblast growth factor, transforming growth factor or epithelial growth factor (see e.g. col 2, line 39-47 and col 3, line 24-41) and DNA. While the growth factors are not explicitly disclosed as DNA encoding the growth factors, it would be apparent to one of ordinary skill in the art that gene delivery of the growth factors is within the scope of the teachings of Coffee et al as Coffee teaches that DNA can be used in his method, and that DNA is known to encode for growth factors and in this form is used routinely in the prior art for expression of growth factors in target cells.. Coffee et al teach that the DNA is encapsulated in liposomes or lipids (bridging paragraph, col 3-4). While the material of Coffee is a wound-covering agent all in its own, the specification contemplates complexing the composition with conventional bandages or dressings (see e.g. col 3, line 50-54). The instant specification teaches that early wound closure decreases the hypermetabolic response, which is inherently loss of lean body mass and compromised immune response. Hence, by closure of the wound by the method of Coffee for treating burn injuries, the hypermetabolic response would be treated as recited in claims 25-27. Coffee et al teach injection into the thermal injury site and injection of the lipid containing DNA into the material (col 3, line 3-40). As the dressing or fibers are administered to the burn, it would indicate that the injection is after thermal injury as recited in claim 30. Severe trauma burn injuries are contemplated such as from battle wounds or motor vehicle accidents, which inherently encompasses second and third degree burns as recited in claims 40-42 (see e.g. col 9, line 15-27).

Coffee does not teach that the lipid is a cholesterol containing cationic liposome as a carrier or vector for the growth factor encoded DNA, nor does Coffee teach explicitly the types

of wound dressings or closure materials as recited in the Markush group of the claimed invention.

It would have been obvious for one of ordinary skill in the art to have employed cholesterol-containing cationic liposomes as carriers or vectors of the DNA of Coffee so as to enhance the wound healing process of an external wound (bone rupture, ligament wound, thermal wound, or external wounds as a result of any trauma known in the prior art) in an individual. One of ordinary skill in the art would have been motivated to have employed the liposomes employed in the cited references because McDonald et al and Yang et al are two of many prior arts of record, which teaches that cholesterol-containing cationic liposomes are routinely employed in the art as effective carriers of therapeutic materials or wound enhancing growth factor encoding gene construct to enhance an efficacy of gene expression of the gene construct at its target site.

Thus, the claimed invention as a whole was *prima facie* obvious.

Claims 5-9, 25-35 and 39-42 are rejected under 35 U.S.C 103(a) are rejected under 35 U.S.C. 103 as being unpatentable over Coffee (US Pat No. 6,252,129; see entire document) taken with McDonald et al. (US Pat No. 6,120,799) or Yang et al (Neuroreport, Vol 8, pages 2355-2358, 1997; see entire document) and further in view of anyone of Baur (US Pat No. 4,361,552), Boyce (US Pat No. 5,976,878), Kushner (US Pat No. 5,741,509), and applicant's admission over the prior art on page 29 of the specification. **This is a new rejection.**

Coffee taken with Yang et al is applied here as indicated above. Coffee taken with McDonald et al do not teach explicitly the types of wound dressings or closure materials as recited in the Markush group of the claimed invention, human fetal amnion.

However, Baur, Boyce, Kushner, and applicant 's admission over the prior art are exemplified references which teach that it is routine in the art at the time the invention was made for one of ordinary skill in the art to have employed wound dressing materials and/or wound closure materials including human fetal amnion on an external wound of an individual so as to enhance the wound healing of the wound.

It would also have been obvious for one of ordinary skill in the art to have further incorporated the liposomal composition of the combined cited references in a wound dressings and/or wound closure material as described in the cited references in order to enhance the wound healing process in any individual having an external wound. One of ordinary skill in the art would have been motivated to have employed the wound dressings and/or wound closure materials as wound healing agents because of the advantages as disclosed in Coffee, Baur, Boyce, and, Kushner, and because Coffee teaches that an enhancement of wound healing processes can be generated using a wound coverage material comprising therapeutic DNA. One of ordinary skill in the art would have a reasons expectation of success to practice the claimed invention particularly in view of the working examples and/or disclosures of the combined cited references, and given the state of the art as a whole, as exemplified by the combined cited references.

Thus, the claimed invention as a whole was *prima facie* obvious.

Claims 5-9, 25-42 are rejected under 35 U.S.C 103(a) are rejected under 35 U.S.C. 103 as being unpatentable over Coffee (US Pat No. 6,252,129; see entire document) taken with Yang et al (Neuroreport, Vol 8, pages 2355-2358, 1997; see entire document) and further in view of anyone of Baur (US Pat No. 4,361,552), Boyce (US Pat No. 5,976,878), Kushner (US Pat No. 5,741,509), further in view of Burgess et al (US Pat NO. 6,559,119; see entire document). **This is a new rejection.**

Coffee taken with Yang et al Baur, Boyce, Kushner, are applied here as indicated above.

However, the combination of the cited references does not teach use of insulin growth factor, keratinocyte growth factor or growth hormone in the method of wound covering of thermal injuries.

Burgess et al teach that a variety of growth factors are essential for wound healing such as from burns and teach administration of insulin growth factor, keratinocyte growth factor or growth hormone to wounds such as burns (see e.g. col 11, line 23-57, col 26, line 36-45 and col 71 line 25-36). Burgess teaches that when a tissue is injured, polypeptide growth factors are released into the wound where they play a crucial role for healing (see e.g. col 2, line 1-16 and col 8, line 13-29).

It would also have been obvious for one of ordinary skill in the art to have further incorporate insulin growth factor, keratinocyte growth factor or growth hormone into the liposomal composition wound dressings and/or wound closure material as described in the cited references in order to enhance the wound healing process in any individual having an external wound. One of ordinary skill in the art would have been motivated to have employed growth factors because of the advantages as disclosed in Burgess et al, and because Coffee teaches that

an enhancement of wound healing processes can be generated using a wound coverage material comprising therapeutic DNA. One of ordinary skill in the art would have a reasons expectation of success to practice the claimed invention particularly in view of the working examples and/or disclosures of the combined cited references, and given the state of the art as a whole, as exemplified by the combined cited references.

Thus, the claimed invention as a whole was *prima facie* obvious.

Response to Argument

Applicants traverse the claim rejections under 35 U.S.C. 103 on pages 6-10 of the amendment filed 9/16/05. Applicants' argue that Goldstein et al is limited to naked DNA and in fact teaches away from complexing DNA with liposomes. As to McDonald et al applicants argue that McDonald does not teach direct application of cationic liposomes into wound coverage materials and in fact teaches away from the instant invention as it teaches that angiogenic endothelial cells in vascular tissue preferably take up the liposomes.

Applicants' response has been considered but is not persuasive for the following reasons. Goldstein et al by teaching use of naked DNA does not teach away from complexing of the DNA with liposomes. In fact there are no explicit teachings in Goldstein et al that suggests that the DNA must be naked. The passage cited by applicants' in column 8, line 52-56 in context simply speaks to the surprising discovery of the inventors that application of DNA to repair cells involved in wound healing by application of the DNA complexed with a wound coverage material leads to extremely efficient uptake of the DNA. There is no indication that the surprising effect is due to the nature of the DNA and that is naked. Rather the prior art teaches

that association of DNA with cationic liposomes comprising cholesterol is responsible for enhanced transfection *in vivo.* Given that this was well-known in the art, a person of skill in the art would have been motivated to further associate the DNA with the cholesterol containing liposomes to further enhance transfection of the repair cells. Applicants have argued that McDonald is limited to angiogenic cells, which teaches away from use of the liposomes in non-angiogenic cells. However, McDonald teaches that in their configuration, uptake by angiogenic cells is enhanced over non-angiogenic endothelial cells. The teachings of McDonald et al do not teach that non-angiogenic cells cannot take up the liposomes, a fact that is confirmed by the prior art (see e.g. Yang et al) which teaches that a variety of cell types are efficiently transfected using cholesterol containing liposomes. As well, angiogenic cells would be expected to be involved in any repair process as these cells are associated with repair processes (see e.g. col 2-3, McDonald et al). Hence in any wound-healing event, delivery to angiogenic cells is within the limits of the instant invention.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria B. Marvich, PhD whose telephone number is (571)-272-0774. The examiner can normally be reached on M-F (6:30-3:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, David Nguyen, PhD can be reached on (571)-272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Maria B Marvich, PhD
Examiner
Art Unit 1633

May 15, 2006

DAVE TRONG NGUYEN
SUPERVISORY PATENT EXAMINER